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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/036,129	12/26/2001	Rajneesh Taneja	ABB1259P0072US (6762.US.0	3432

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EXAMINER	
SHEIKH, HUMERA N	
ART UNIT	PAPER NUMBER
1615	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/036,129	TANEJA ET AL.	
	Examiner	Art Unit	
	Humera N. Sheikh	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 May 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,9-21 and 23-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,9-21 and 23-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

Receipt of the Request for Continued Examination (RCE) under 37 CFR §1.114 and Applicant's Arguments/Remarks, both filed 05/29/07 is acknowledged.

Claims 1-7, 9-21 and 23-36 are pending in this action. No claims have been amended herein. Claims 8 and 22 have previously been cancelled. Claims 1-7, 9-21 and 23-36 are rejected.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 05/29/07 has been entered.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

The instant invention is drawn to a method for treating gastric acid disorders comprising the step of administering to a patient in need of such treatment a therapeutically effective amount of at least one non-enteric coating proton pump inhibitor in a pharmaceutically acceptable carrier; wherein said pharmaceutically acceptable carrier comprises an equimolar ratio of a bicarbonate salt of a Group IA metal and a carbonate salt of a Group IA metal where the Group IA metal is chosen from the Periodic Table of Elements.

Claims 1-7, 9-21 and 23-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Phillips (US Pat. No. 6,489,346 B1) (hereafter 'Phillips I').

Phillips I ('346) teaches a method for treating acid-related gastrointestinal disorders comprising administering to a patient a non-enteric pharmaceutical composition comprising a non-enteric coated proton pump inhibitor in a pharmaceutically acceptable carrier and at least one buffering agent, wherein the pharmaceutically acceptable carrier comprises a bicarbonate salt of a Group IA metal and a carbonate salt of a Group IA metal (see Abstract; Claims); (col. 11, lines 36-44); (col. 13, line 47 – col. 14, line 26).

At column 13, lines 47-53, Phillips teach that mixtures of the buffering agents can be utilized. Suitable buffering agents disclosed include sodium bicarbonate, potassium bicarbonate,

aluminum hydroxide/sodium bicarbonate co-precipitate and sodium carbonate (see col. 13, line 63 – col. 14, line 14); (col. 17, lines 58-60). Potassium carbonate is disclosed at column 22, lines 7-8. Sodium bicarbonate is provided in amounts of about 1000 mg to about 1680 mg (see claim 17). This amount range is an overlapping range, which meets the instantly claimed range of about 125 mg to about 1000 mg of sodium bicarbonate.

The non-enteric proton pump inhibitors include a substituted benzimidazole of lansoprazole or salts thereof (see Abstract). Example IV at column 22, lines 1-39 demonstrates an effervescent formulation whereby omeprazole powder was diluted with sodium bicarbonate, citric acid and potassium carbonate to form a homogeneous mixture of omeprazole powder.

With regards to the instant amounts, such as the 'equimolar ratio of a bicarbonate salt of a Group IA metal and a carbonate salt of a Group IA metal' and an 'equimolar ratio of sodium bicarbonate and sodium carbonate', Phillips does not explicitly teach 'equimolar ratios of a bicarbonate and carbonate salt of Group IA metals. However, the Examiner points out that generally, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller,* 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). In this instance, prior art teaches the use of the same drug (PPI) and the same components (buffer – (bi)carbonates, carrier) in similar dosage forms (tablets, capsules) to effectively treat conditions of gastric acid disorders in a subject in need thereof. Furthermore, it is deemed obvious to one of ordinary skill in the art to determine suitable or effective amounts through the use of routine or manipulative experimentation to

obtain optimal results, as these are indeed variable parameters attainable within the art. Absent evidence to the contrary, the instant 'equimolar ratios' as claimed fail to impart any unexpected results. The prior art addresses the concern of avoiding large amounts of bicarbonate or other buffers, to overcome any adverse effects (*i.e.*, frequent belching) by administering a single dose, which does not require any further administration of a bicarbonate (see col. 9, line 28 – col. 10, line 14); (col. 13, lines 7-27).

Thus, given the teachings of Phillips ('346) who teaches a method for treating gastric disorders by administering carbonates and bicarbonates in combination with proton pump inhibitors, the instant invention, when taken as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 1-7, 9-21 and 23-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Phillips (US Pat. No. 5,840,737) (hereafter 'Phillips II') in view of Phillips (US Pat. No. 6,489,346 B1) (Phillips I).

The instant invention is drawn to a method for treating gastric acid disorders comprising the step of administering to a patient in need of such treatment a therapeutically effective amount of at least one non-enteric coating proton pump inhibitor in a pharmaceutically acceptable carrier; wherein said pharmaceutically acceptable carrier comprises an equimolar ratio of a bicarbonate salt of a Group IA metal and a carbonate salt of a Group IA metal where the Group IA metal is chosen from the Periodic Table of Elements.

Phillips II ('737) teaches a method for treating gastric acid disorders by administering to a patient a single dose of a pharmaceutical composition including an aqueous solution/suspension of proton pump inhibitors – omeprazole, lansoprazole or other substituted benzimidazoles and derivatives thereof in a pharmaceutically acceptable carrier wherein the carrier comprises a bicarbonate salt of a Group IA metal (see abstract and claims). Phillips also teaches a pharmaceutical composition, which includes omeprazole or other substituted benzimidazoles and derivatives thereof in a pharmaceutically acceptable carrier wherein the carrier comprises a bicarbonate salt of a Group IA metal (see abstract and claims).

Phillips II teaches a method for treating gastric acid disorders wherein the Group IA metal is sodium and potassium (see claims 1-3).

It is stated that the pharmaceutical composition is prepared by mixing omeprazole or other substituted benzimidazoles and derivatives thereof with a solution including a bicarbonate salt of a Group IA metal. Preferably, omeprazole powder or granules are mixed with a sodium bicarbonate solution to achieve a desired final omeprazole concentration (col. 7, line 50 through col. 8, line 5).

Phillip II states that the pharmaceutically acceptable carrier includes the bicarbonate salt of the Group IA metal and can be prepared by mixing the bicarbonate salt of the Group IA metal, which is preferably sodium bicarbonate, with water. The concentration of the bicarbonate salt of the Group IA metal in the composition generally ranges from approximately 5.0% to about 60%. In a preferred embodiment, the preferred salt is sodium bicarbonate and is contained in a concentration of about 8.4% (col. 8, lines 6-17).

Suitable derivatives of omeprazole can be substituted for the omeprazole or other suitable substituted benzimidazoles, wherein these derivatives include lansoprazole (col. 8, lines 41-45).

The pharmaceutical composition can be used for the treatment of gastrointestinal conditions, including, active duodenal ulcers, gastric ulcers, gastroesophageal reflux disease (GERD), severe erosive esophagitis, poorly responsive systematic GERD, and pathological hypersecretory conditions (col. 8, lines 46-61).

The examples on columns 10-19 further demonstrate various embodiments of the invention in greater detail.

Additional agents that can be added include antimicrobial preservatives, antioxidants, chelating agents and buffers (column 9, lines 23-26).

While Phillips II does not explicitly teach the instant amounts, such as the 'equimolar ratio of a bicarbonate salt of a Group IA metal and a carbonate salt of a Group IA metal' and an 'equimolar ratio of sodium bicarbonate and sodium carbonate', the Examiner points out that generally differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). Applicants have not demonstrated any unusual/unexpected results that accrue from the instant equimolar ratios. It is deemed obvious to one of ordinary skill in the art that suitable ratios and/or amounts could be determined through the use of routine or manipulative experimentation to obtain the best possible results, as these are indeed variable parameters obtainable within the art. The prior art vividly recognizes the need to

administer lower amounts of bicarbonate to avoid adverse effects in gastroesophageal patients. Thus, the Phillips II reference meets the same objectives desired by Applicants.

Regarding the 'non-enteric' proton pump inhibitor claimed by Applicant, Phillips II teaches a method for treating gastric acid disorders whereby the use of enteric coatings can be used if desired, indicating that enteric coatings are optional. Furthermore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to either employ enteric coatings if drug delivery in the intestines was desired or alternatively, to exclude enteric coatings if delivery of drug to the stomach was desired. The expected result would be a drug formulation having distinct rates of release.

Phillips II ('737) does not teach a *carbonate* salt of the Group IA metal.

Phillips I ('346) teaches a method for treating acid-related gastrointestinal disorders comprising administering to a patient a non-enteric pharmaceutical composition comprising a non-enteric coated proton pump inhibitor in a pharmaceutically acceptable carrier and at least one buffering agent, wherein the pharmaceutically acceptable carrier comprises a bicarbonate salt of a Group IA metal and a *carbonate salt of a Group IA metal,* whereby suitable buffering agents include sodium carbonate, for example (see Abstract; Claims); (col. 11, lines 36-44); (col. 13, line 47 – col. 14, line 26).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include the carbonate salt of the Group IA metal of Phillips I ('346) within the teachings of Phillips II ('737) who teaches bicarbonate salts of the Group IA metal

because Phillips I explicitly teaches a proton pump inhibitor formulation comprising suitable buffering agents of both carbonates and bicarbonates of Group IA metals and teaches that the buffering agents (*i.e.*, carbonates/bicarbonates) function to substantially prevent or inhibit acid degradation of the proton pump inhibitor by elevating pH of the stomach sufficiently to achieve adequate bioavailability of the drug to effect therapeutic action. The expected result would be a non-enteric coated formulation wherein the bioavailability of the proton pump inhibitor is preserved to provide for the effective treatment and/or prevention of gastric acid related disorders.

Response to Arguments

Applicant's arguments filed 05/29/07 have been fully considered, but were not found to be persuasive.

- **35 U.S.C. §103(a) Rejection of Claims 1-7, 9-21 and 23-36 over Phillips I ('346):**

Applicant argued, "Phillips I does not expressly or inherently teach the equimolar ratio of a bicarbonate salt of a Group IA metal and a carbonate salt of a Group IA metal. Similarly, Phillips I does not teach an equimolar ratio of sodium bicarbonate and sodium carbonate. There is nothing in Phillips I that discloses or suggests to a skilled artisan to select a combination of a bicarbonate salt of a Group IA metal and a carbonate salt of a Group IA metal in an equimolar ratio out of all the possible buffer combinations."

These arguments have been considered but were not found to be persuasive. Admittedly, the Phillips I reference does not explicitly teach an equimolar ratio of a Group IA metal and a carbonate salt of a Group IA metal. However, the difference in the ratio amounts between the instant invention and the prior art does not render a patentable distinction over the reference teachings. Suitable or effective amounts or ratios can be determined by one of ordinary skill in

the art through routine or manipulative experimentation to obtain optimal results, as these are variable parameters attainable within the art. Moreover, the Examiner points out that generally, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller,* 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). In this instance, the prior art provides for similar methods for treating gastrointestinal disorders as instantly claimed herein.

Applicant argued, "It is known in the art that sodium bicarbonate produces gas while neutralizing stomach acids. The formation of this case causes distension of the stomach, which results in a bloated feeling, belching and flatulence. Also, it is also known in the art that sodium biocarbonate ingestion can cause the spontaneous rupture of the stomach. Throughout the specification, the superior results attributable to the equimolar ratio of sodium carbonate and sodium bicarbonate ("carbicarb") are discussed and provided for, namely, the reduction in the comparative amounts of gas, including CO_2 gas that is produced. This reduction in gas reduces the distension of the stomach, belching and flatulence experienced by patients who take the compositions of the present invention when compared to patients who take compositions containing solely sodium bicarbonate (such as those disclosed in Phillips I and II)."

Applicant's arguments have been considered, but were not persuasive. The amounts of sodium bicarbonate taught in the art, such as about 1000 mg, would be considered a suitable and effective amount, which would also provide for reduction in gas formation, thus leading to reduction in stomach distension, belching and flatulence, as is desired by Applicant. Applicants recite an equimolar ratio of sodium carbonate to sodium bicarbonate in order to reduce distension of stomach, belching and flatulence. It is noted that the prior art is also aimed at concerns of avoiding large amounts of bicarbonate or other buffers, to avoid or overcome adversary effects, such as frequent belching. Thus, the prior art achieves the same objectives as that intended by

Applicants. It is the position of the Examiner that the instant claims remain generic enough to read on the teachings of the prior art.

Applicant argued, "Applicants believe that they have demonstrated that the particular range is critical. There is simply no teaching or suggestion anywhere in Phillips I that an equimolar ratio works better than other possible buffer combinations. Furthermore, the kind of improvement includes the prevention of stomach rupture and other gas-related maladies."

These arguments were not persuasive. Applicant's arguments do not establish the scope of claims being presented. The claims are generic in terms of what particular types of conditions or maladies can be treated and are not species-specific with regards to treating specific conditions or disorders. Thus, Applicant's arguments do not represent the scope of the instant claims. Moreover, the claims at present are silent with regards to the levels of gas reduction desired and/or specific amounts of gastric fluid that can be neutralized.

- **35 U.S.C. §103(a) Rejection of Claims 1-7, 9-21 and 23-36 over Phillips II ('737) in view of Phillips I ('346):**

Applicant argued, "Phillips I does not teach the equimolar ratio of a bicarbonate salt of a Group IA metal and a carbonate salt of a Group IA metal. While Phillips I discloses a broad mixture of possible buffering agents, there is no teaching or suggestion to use the equimolar mixture, specifically carbicarb. Phillips II is directed to a method of treating gastrointestinal conditions by administering omeprazole in a carrier with a bicarbonate salt of a Group IA metal, wherein the administration step consists of a single dosage. Therefore, a skilled artisan would not be motivated to replace the bicarbonate salt of a Group IA metal with an equimolar mixture of carbonate and bicarbonate."

These arguments were not persuasive. While an "equimolar ratio" is not expressly taught in the Phillips references, the fact that Applicant incorporates a slightly different amount than that of the prior art, does not render a patentable distinction, since the art is clearly directed to formulations and methods of treating gastrointestinal diseases, whereby the formulations are substantially comprised of essentially the same components as that implemented by Applicants. Effective amounts can be determined by routine optimization by one having ordinary skill in the art. In addition, the prior art formulations and methods are directed to providing an effective reduction in belching, as is also desired by Applicants.

Hence, the instant invention, when taken as a whole, would have been *prima facie* obviousness to one of ordinary skill in the art at the time the invention was made.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Humera N. Sheikh whose telephone number is (571) 272-0604. The examiner can normally be reached on Monday, Tuesday, Thursday and Friday during regular business hours. (Wednesdays - Telework).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Humera N. Sheikh

Primary Examiner

Art Unit 1615

August 16, 2007

HUMERA N SHEIKH
PRIMARY EXAMINER

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